



## **CLEAN VERSION OF PENDING CLAIMS**

### **METHOD OF IDENTIFYING INHIBITORS OF TOPOISOMERASE DNA RELIGATION**

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1. (Amended) A high-throughput method of screening compounds capable of modulating topoisomerase activity comprising:

(a) incubating at least a first nucleic acid, a topoisomerase and a potential topoisomerase-modulating compound, wherein the nucleic acid comprises at least one tag, and

(b) assaying for a nucleic acid religation product.

2. The method of claim 1, wherein the nucleic acid is DNA.

3. The method of claim 1, wherein the nucleic acid is RNA.

4. The method of claim 1, wherein the at least one tag is a detection tag or an affinity tag.

5. The method of claim 1, wherein the method comprises incubating at least a first nucleic acid and a second nucleic acid.

6. The method of claim 5, wherein the second nucleic acid is a religation strand comprising oligonucleotides operatively associated with at least one marker tag.

7. The method of claim 6, wherein the first nucleic acid is operatively associated with an affinity tag and the second nucleic acid is operatively associated with a detection tag.

8. The method of claim 1, wherein the assay detects for topoisomerase inhibitors

9. The method of claim 1, wherein the assay detects for topoisomerase activators.

10. The method of claim 1, wherein the topoisomerase is a Type I or Type III topoisomerase.

11. The method of claim 1, wherein the topoisomerase is a Type II or Type IV topoisomerase.

12. The method of claim 1, wherein assaying comprises measuring the level of nucleic acid religation activity in the presence and absence of the topoisomerase-modulating compound

13. The method of claim 1, wherein the level of religation activity is inversely proportional to the effectiveness of the topoisomerase-inhibitory compound.

14. The method of claim 1, wherein step (a) is performed on a solid support.

15. The method of claim 1, wherein step (a) is performed in a liquid phase.

16. The method of claim 1, wherein the nucleic acid and topoisomerase are covalently complexed, wherein the topoisomerase retains its religation activity.

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20. (Amended) A kit for screening compounds that modulate topoisomerase religation activity comprising:

- (a) a substrate nucleic acid comprising a first tag,
- (b) a religation nucleic acid comprising a second tag and a 5'-OH,
- (c) a topoisomerase, and

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(e) a means for measuring a covalently linked product comprising (a) and (b) in a test mixture comprising (a), (b) and (c) in the presence or absence of a topoisomerase-modulating compound.

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22. (New) A method to identify a compound that modulates topoisomerase activity comprising:

(b) incubating a reaction mixture comprising a substrate nucleic acid, a religation strand, a topoisomerase, and a candidate compound; and

(c) assaying for ligation of the substrate nucleic acid and the religation strand.

23. (New) A method to identify a compound that modulates topoisomerase activity comprising:

(c) incubating a reaction mixture comprising a substrate nucleic acid, a topoisomerase, and a candidate compound; and

(d) assaying for intramolecular ligation of the substrate nucleic acid to form a hairpin, a circular nucleic acid, or a multimer of the substrate nucleic acid.

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